THE PSEUDOMALARIAL TYPES OF INFECTIVE ENDOCARDITIS.[1]

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CASES of infective endocarditis simulating malarial fever have been reported from time to time for half a century, yet adequate recognition has scarcely been given to the subject in text-books. Nor has the attempt been made, so far as I am aware, to bring together the various types. The importance of infective endocarditis and the difficulty often encountered in arriving at a correct diagnosis apparently justify a consideration of the pseudomalarial forms under which it may be masked.

Before the discovery of the malarial parasite, especially, the attempt was made to establish an etiological relation between malarial fever and infective endocarditis. It was entirely *post hoc* reasoning. Convincing proof of such relationship has not yet been offered. In fact, it is almost universally conceded that antecedent or coincident malaria is merely fortuitous. Some cases have given histories of recent or old-recurring malarial attacks, but these histories must be accepted with caution, at least in certain instances. The pseudomalarial types of endocarditis are subject to complete, though temporary, interruption for weeks at a time. Herzog has reported the coincident presence of the malarial parasite in one case, but does not prove its etiological significance. It was present also in a fatal case treated at Bellevue, and in another at City (Charity) Hospital.

The cases of infective endocarditis of pseudomalarial type which have been reported fall broadly into two groups, acute and chronic. The duration of the acute cases is measured by weeks, of the chronic by months. It will often be found, however, that cases which have died after a few weeks' observation give histories extending over several months. Other chronic cases may continue for eighteen months or more.

The pseudomalarial must be distinguished from the frankly septic and pyæmic forms of infective endocarditis, of which they constitute a remarkable sub-group. They differ rather in the periodicity than in the nature of the paroxysms. Their resemblance to malarial fever is often very exact. The paroxysms may recur at regular periods, even at the same hour, and the intervals be fever-free. In the apyrexial periods the temperature is often subnormal. No special infective agent is responsible for the pseudomalarial types, nor is it necessary that there shall have been previous cardiac valvular disease.

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The cause of the periodicity has not been determined. It has been thought to be due to disturbance of the heat-regulating mechanism by an antecedent malaria, and that the stamp of malaria is carried by the subsequent febrile movement. This seems unlikely, since no other febrile disease, when it follows a malarial attack, pursues such a course. Nor has it even been proved that the majority of cases have been recently preceded by malaria. Sicard found staphylococci in the blood in the pyrexial but not in the apyrexial periods of one case.

The following pseudomalarial types have been reported:

1. Double quotidian.
2. Quotidian.
3. Tertian.
4. Quartan.
5. Septan.
6. Mixed types.
7. Irregular.

A single case may present during its course several of these types, yet at a particular period each type be pure. It is almost characteristic of these cases that they change their course. In spite of this fact, it is advisable to speak of distinct types. Cases may be under observation for short periods only, during which a definite type is preserved.

When the disease is approaching a fatal termination, the paroxysms often return irregularly.

CHARACTERS OF THE PAROXYSMS. The paroxysms may be identical with those of malarial fever, presenting cold, hot, and sweating stages, with fever-free intervals. The cold stage may be accompanied by a prolonged, hard chill, or simply by sensations of chilliness. As in malaria, the temperature may rise steadily through the chill. The chills begin with or after the initial rise of temperature, which, though sharp, may occupy several hours in reaching its maximum. In acute cases the maximum is often very high, even 107°. The defervescence is sudden and generally marked. The temperature may fall 1° or 2° below normal. Subnormal interval temperatures have occurred in a number of cases. Sweating may be profuse, scanty, or absent. It is commonly present. Vomiting often accompanies a paroxysm. A single paroxysm may occupy from six to eight hours. The intervals between the paroxysms may be fever-free or show a slight febrile movement.

The Onset. The onset is often like a simple malarial attack. The type may be established at once, or only after a period of irregular paroxysms. When first seen the patient may give a history of recent apparent malaria, with apparent relief from quinine. Such a history almost necessarily deceives one at first as to the true nature of the illness. It has probably led also to the false assumption of recent malarial attacks by some authors.

1. Double Quotidian Type.—I have been able to find only one case in which this type was followed unchanged to the fatal termination. The double quotidian type has generally appeared only toward the end of the disease. The previous course may have been quotidian, tertian, or irregular.

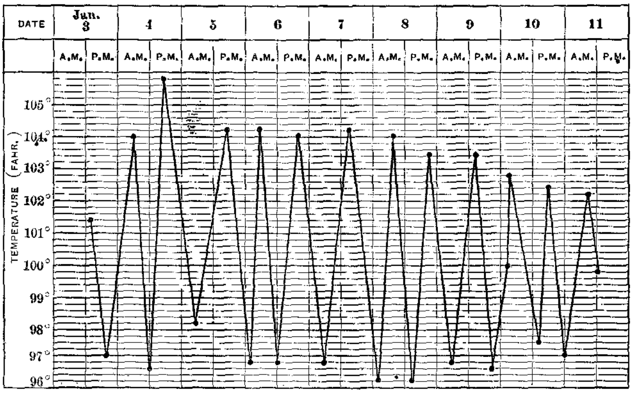
Illustrative Case. Coupland's Case I. Male, aged forty-one years. Gonorrhœa at twenty, otherwise healthy. Took cold two months ago. Next day had pain in left leg, which was relieved by local applications. Patient always felt weak afterward. Five weeks ago began to suffer from "shivering fits," from which he has not since been free. Paroxysms at irregular intervals, some every third day, some every fifteen hours. Thought he had ague. Each attack was accompanied by vomiting and was followed by an intolerable sense of heat. Became progressively weaker. No pain, but noticed latterly that legs swelled toward night.

Status Præsens. Looks very ill; is spare and sallow. Lungs practically normal. Cardiac dulness normal. Rough systolic bruit at apex. No thrill. Pulmonic second sound ringing; aortic dull.

Course. Throughout whole course, pyrexial periods averaged about five hours. Rigors, which sometimes commenced with and sometimes after the initial rise of temperature, averaged one and one-half hours' duration. The apyrexial periods, during which the temperature frequently fell to extreme subnormal levels, averaged ten hours. Absence of sweating was a marked feature.

Fig. 1 represents the double quotidian paroxysms. Fig. 2 represents double quotidian changing into quotidian paroxysms.

Fig. 1.

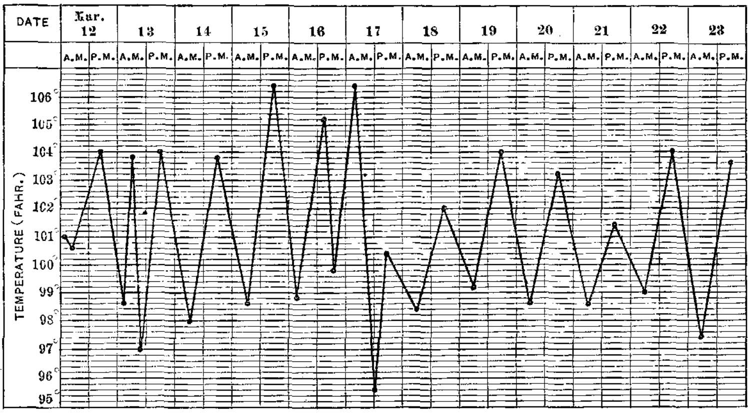


Double quotidian type. Coupland's Case I.

2. Quotidian Type. *Illustrative Cases.* Dock's Case I. (1895). Female, aged twenty-six years. Forceps delivery, with laceration

of perineum. Wound healed quickly. Three weeks later went sleighing. Afterward remained in bed. Had chills, fever, and sweating almost every day.

FIG. 2.



Double quotidian changing to quotidian. Coupland's Case II.

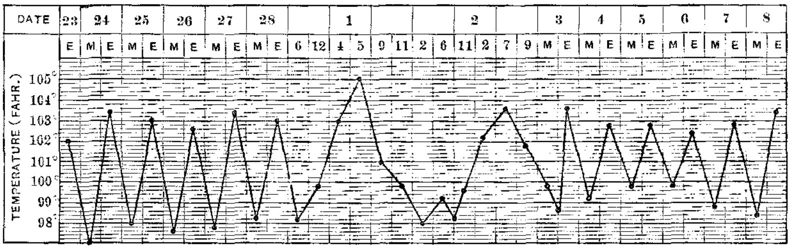
Status Præsens. Slight emaciation. Moderate effusion in right knee. Feet painful, but not swollen. Fugitive painful swellings in fingers. Heart enlarged, impulse heaving, loud mitral systolic murmur. Second sounds normal. No cardiac lesion found at examination prior to administration of chloroform for forceps delivery.

Course. Rise of temperature usually occurred about noon, reached its acme about 5 P.M., sometimes one or two hours later, and after remaining at about the same point for one or two hours fell rapidly, usually reaching normal by midnight. Toward the last subnormal temperatures often occurred. Chills not constant, though very common, coming on early in the rise of temperature and of short duration. Sweating almost always present in the decline. Patient felt well, though weak, during apyrexial periods. Pain in the knees, ankles, feet, and hands, and itching of the skin were frequent. No cutaneous hemorrhages, but urine became bloody shortly before death. Fig. 3 shows the quotidian paroxysms.

Osler has reported two remarkable chronic cases of quotidian type of ten and eleven months' duration.

Osler's Case I. Male, aged forty-three years. Indefinite history of chronic malaria when a young man. Illness began with a chill, followed by fever, malaise, and muscular soreness. Headache, loss of appetite, insomnia, and cough were marked symptoms. Spleen large. Symptoms abated in a few days and patient resumed business. Three weeks later marked dyspnœa, with increasing cough, developed, and a loud systolic murmur was heard at the apex for the first time. Had daily intermittent fever, usually subnormal in the morning, and ranging from 102° to 103° in the evening, with occasional sweats. Pains in different parts of the body, particularly in the left inguinal region; tenderness over the fourth and fifth left costal cartilages. Fever continued throughout winter, with weakness, cough, and dyspnœa. Patient in the Johns Hopkins Hospital from March 15th to May 10th. There were no chills, only slightly chilly feelings. Morning temperature was 97.5° to 98°, with a gradual rise to 102° to 103° at 4 P.M., and a gradual fall to normal at midnight. Between 4 and 5 o'clock in the afternoon, sometimes not until evening, there was sweating, occasionally profuse; more frequently the skin was only slightly moist. The general condition improved somewhat, and the patient gained slightly in weight. The only complaint was pain in the splenic region, sometimes with very distinct tenderness. There was no change in the cardiac condition while in the hospital. The temperature range was low, and often subnormal toward the end. Petechiæ appeared. Sweating continued. The patient failed progressively. Diarrhœa developed. The urine contained blood and blood casts. Death.

FIG. 3.



Quotidian type. Dock's Case I. (1895). Portion of chart.

3. TERTIAN TYPE. *Illustrative Case.* Elsner's Case I. Symptoms of intestinal infection for several days. At the same time had a persistent gonorrhœal discharge. Without marked disturbances of any kind, without evidences of constitutional infection, patient suddenly developed a tertian form of intermittent fever, and ague was suspected. It became evident after the third day that the prostration was greater than in malaria, the delirium more marked, and nervous symptoms more profound. There was increasing shortness of breath. Heart rapid, sounds suggestive of mitral insufficiency. Spleen large. Albuminuria. After the third chill, in spite of the fact that the tertian type of fever persisted, the temperature was always slightly elevated. Physical signs of auriculoventricular insufficiency, with aortic stenosis. Death in fourth week, in typhoid

condition, with hemiplegia, occasional chills, and sharp rises of temperature. Fig. 4 shows tertian paroxysms.

4. QUARTAN TYPE. *Illustrative Case.* Wenckelbach. Male, aged fifteen years. Entered eye clinic, after measles, for interstitial keratitis. Developed intermittent fever, complained of palpitation. Heart enlarged; sounds clear, but accentuated. Fever followed quartan type. Intervals not fever-free. No malarial parasites in blood. Daily attacks of palpitation, up to 160 per minute. Heart still further enlarged. Spleen enlarged, with piercing pains. Staphylococcus albus obtained from blood. Diagnosis, infective endocarditis. Cured after injections of collargol. Fig. 5 shows quartan paroxysms.

5. SEPTAN TYPE. *Illustrative Case.* Henry. Female, aged nineteen years. Typhoid three years ago, rheumatism in childhood, pneumonia a few months ago. Pregnant. Well-compensated mitral obstruction. Repeated examinations of blood for malarial parasite gave negative result. Rise of temperature accompanied on two occasions by chill, once by vomiting. "The inference that the fever is dependent on the heart lesion is based on the fact that no other cause could be found for it." Patient recovered.

This case is the only one of pure septan type that I have been able to find, though septan paroxysms have occasionally occurred toward the end of cases which at other times had followed other types. Fig. 6 shows the septan type.

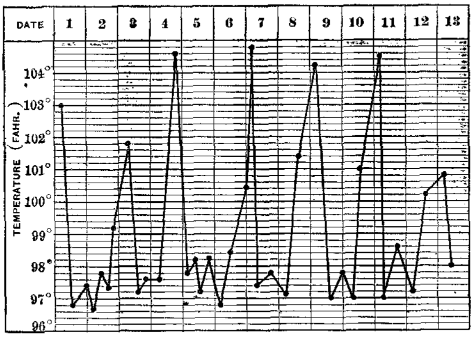
6. MIXED TYPES. These may be dismissed with a few words. The term is employed to designate only those cases which present two different types simultaneously. Such cases must be extremely rare. I have not been able to find even one which followed this course uninterruptedly. However, since Finlayson's case presented mixed tertian and quartan paroxysms during two months of its course, it seemed necessary to include the "mixed types." Fig. 7 is a part of the temperature chart of Finlayson's case.

7. IRREGULAR TYPES. The irregular types constitute by far the majority of cases of infective endocarditis which bear resemblance to malarial fever. The resemblance rather dates back to the time, however, when exact knowledge of the malarial parasite had not been acquired—when cases were diagnosticated as malarial fever simply because of recurring periods of pyrexia. No less an authority than Dreschfeld states, in Allbutt's *System of Medicine,* that all cases of chronic infective endocarditis resemble malarial fever. Such a statement is, to say the least, unfortunate.

The irregular acute cases are generally so clearly septic and the constitutional symptoms so marked that there is little difficulty in recognizing them, while the chronic cases are generally so irregular and so frequently develop in the course of chronic cardiac valvular disease that one is not left long in doubt as to their real nature.

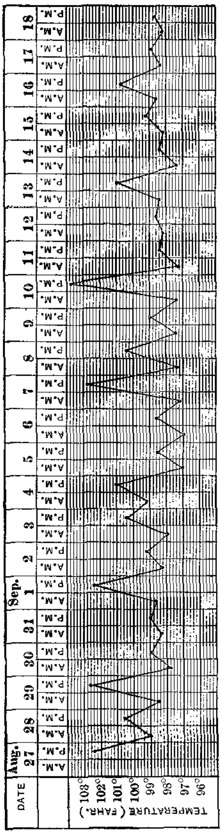
Diagnosis. The diagnosis of a pseudomalarial form of infective endocarditis is often very difficult. As in other varieties, the heart

FIG. 4.



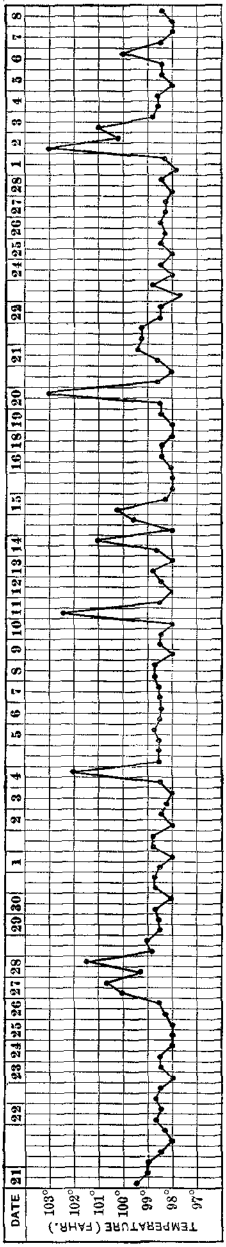
Tertian type. Portion of chart of Finlayson's case.

FIG 5.



Quartan type. Wenckelbach's case.

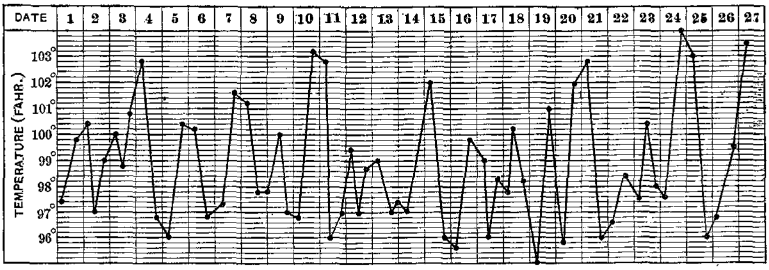
FIG. 6.



Septan type. Henry's case.

may give neither signs nor symptoms. If the infective process has been engrafted upon an old valvular lesion, the diagnosis need not present much difficulty, nor if an atrium of infection can be found. But the cryptogenic cases, occurring in persons previously healthy, or in those who, living in suspicious localities, give histories of recent apparently malarial attacks, may severely tax the skill of the clinician. As already mentioned, the disease is subject to sudden and complete, though temporary, interruptions. The patient may have been taking quinine. Under the circumstances, what is more natural than to assume that the quinine has stopped the paroxysms, even though the blood may not have shown the malarial organisms? When the patient returns for treatment, or if he comes with such a history, the existence of malarial infection is presumptive, and the case may go unrecognized, at least for a time. Then the failure of quinine to mitigate or arrest the paroxysms gives the first intimation that the patient is not suffering from malaria—assuming, of course, that a complete examination of the blood has not been made. Such an examination will at once rule out malaria, but, on the other hand, the presence of the malarial parasite does not necessarily exclude infective endocarditis (*vide* Herzog's case).

FIG. 7.



Mixed tertian and quartan types. Portion of chart of Finlayson's case.

In infective endocarditis there is generally though not always leukocytosis; in malaria, leukopenia is the rule, except during a paroxysm. In infective endocarditis the polynuclear leukocytes are increased; in malaria there is relative lymphocytosis. Pigmented leukocytes are found in nearly all severe and protracted or fatal cases of malaria. The red cells and hæmoglobin show much the same changes in both conditions—rapid, marked oligocythæmia, hæmoglobin reduction, and degenerative changes in the cells. The changes are essentially those of secondary anæmia, though sometimes in malaria they pass into the pernicious type. The recovery of the infective agent from the blood is often possible and always conclusive, provided no other nidus than the heart valves can be found.

One of the remarkable features of these forms of infective endocarditis is the strength of the patient between the paroxysms. Until the disease is advanced he may feel quite well, and the classical picture of sepsis be lacking. Changes of type commonly occur during the course of the disease, and should be of much aid in diagnosis. In Ord's case, for example, the type changed from quotidian (two weeks) to tertian (two weeks), then to quartan, and later became irregular, the paroxysms recurring sometimes at intervals of a week. If an obstructive valvular lesion develops in a case pursuing a malarial course, the disease is almost certainly infective endocarditis. But, after all has been said, many cases will prove difficult to diagnosticate.

Pathological Anatomy. The simulation of malaria by infective endocarditis appears again in manycases in the pathological anatomy and histology of the viscera. In both diseases the long-continued hæmolysis results in the deposit of pigment in the spleen, liver, and bone-marrow, and while in malaria this pigmentation is much more extensive, owing to the activity of the parasites, nevertheless, the pigmentation of the viscera seen in septic processes often reaches a grade quite comparable to that of malaria. Thus, the spleen in septic processes may be considerably enlarged, distinctly brownish in color, and in very acute cases nearly diffluent. Likewise, the liver may exhibit a brownish or leaden color, much like that of malaria. Histologically, there is the same filling of endothelial cells of pulp and capillaries with masses of granular and globular pigment, the minute morphology of which is very similar in both malaria and infective endocarditis with bacteræmia. Hence it is unsafe to attempt to distinguish malaria from septic processes merely on the gross or microscopic appearance of pigment in the viscera. The only reliable method is the demonstration of the bodies of malarial parasites in cases of this disease, and their absence in septic processes. In nearly all other respects the pathological anatomy of pernicious malaria may be closely reproduced by septicæmia.

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DISSEMINATED SYPHILITIC ENCEPHALITIS.

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The following study is of a case of syphilis of the central nervous system, which presents points of interest in its pathological histology and as an example of the occurrence of severe syphilis of the nervous system soon after infection, at a time when the constitutional symptoms were still marked. There occur in the nervous system a variety of lesions, some of which may be regarded as specific; others cannot be differentiated from simple inflammatory phenomena. These inflammatory phenomena occur throughout the entire cortex, and also as focal areas of granulation tissue. These latter so overshadow the other features that it seems best to designate the case one of disseminated syphilitic encephalitis.

Summary of the Clinical History. C. C., male, aged forty-one years, admitted to the Danvers Insane Hospital, December 11, 1902. Family and early personal history not noteworthy. While not a steady drinker, he occasionally used alcohol to excess. June 12, 1902 he consulted a physician, giving a history of syphilitic infection three weeks previous, and then showed an initial lesion on the dorsum of the glans penis. On July 2, he was again seen by the same physician at a time when just recovering from an alcoholic debauch. The primary sore then showed extensive ulceration, and there was a papular eruption over the arms, chest, abdomen and legs. He was put upon a specific treatment of mercury, with occasional weeks of mixed treatment. An attack of iritis occurred, but soon disappeared with increased dosage. In the latter part of November, or about six months after infection, he had severe headaches which could be only partially controlled by treatment. Soon he became forgetful and was described as being "stupid." He was neglectful of his personal habits and "too stupid to eat." This condition led to his commitment to this hospital.

The examination made at his admission by Dr. Mitchell shows that he was poorly nourished, weighing 124 pounds. He was so